REMARKS

Applicants respectfully request reconsideration of the claims pending in this application. Claims 1-21 are pending. Claims 20 and 21 are withdrawn from consideration. Claims 1-19 stand rejected. By the above amendment, Applicant amends claims 1-3, and 13-17 in order to more specifically describe the present invention. Additionally, claims 4, 5, and 18 are canceled and new claims 22-25 are added. In the remarks that follow, Applicants address each of the issues raised in the in the order in which they appear in the Office Action mailed July 24, 1998.

Applicants affirm the election of claims 1-19.

Additionally, Applicants acknowledge the CRF correction by the STIC Systems Branch.

The Examiner has rejected claims 1, 2, 4, 5, 18 and claims dependent from these claims, under 35 U.S.C. §112, first paragraph, as containing subject matter not described in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. With respect to claims 1, 4, 5 and 18 the Examiner asserts that without knowing what an "AIR" polypeptide is, one cannot make a number of species, commensurate in scope with the claims. Applicants respectfully traverse this rejection and submit that these claims unambiguously and definitely define the present invention, and meet all of the requirements of Section 112. Amended Claim 1(a) and (b) recite DNA that encodes specific amino acids of defined sequences. Claim 1(c) recites DNA that hybridizes under specifically stated conditions to specific DNA, **AND** encodes biologically active apoptosis inducing receptor. Similarly, claim 1(d) recites DNA that encodes biologically active fragments of the DNA of (a), (b), and (c). Claims 4, 5, and 18 are canceled and new claims 22 and 24 and 25 added in their stead. As discussed below, one ordinarily skilled in the art, in view of the specification and the state of the art, is able to make and use the claimed compounds.

Applicants disagree with the Examiner's position and respectfully submit that the present specification clearly describes 1) the claimed specific sequences; 2) the claimed hybridization conditions; 3) methods for testing the biological activity of polypeptides that are included within the structural definition of claim 1(c) and 1(d); and, 4) methods for preparing and testing polypeptide and DNA variants and derivatives. More particularly and with respect to claim 1(c) and 1(d), specific hybridization conditions are described on page 9 of the specification, and, starting at page 5 and continuing through page 9, the specification describes methods for preparing polypeptides derivatives, variations and mutants. Additionally, beginning on page 9, the specification describes methods for testing the ability of polypeptide variants, derivatives and mutants to cause apoptosis of cells, or, in the case of some fragments and fragment muteins, to inhibit apoptotic induced cell death.

The Examiner appears to be of the opinion that the standard for enablement requires that all possible embodiments embraced by the claims be described. Applicants submit that

the Examiner is mistaken and is improperly rejecting these claims. The standard is whether a person skilled in the art is able to make the embodiments and determine which embodiments would be inoperative or operative, without undue experimentation, using the state of the art and applicants' written disclosure. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is routine experimentation.

As stated above, the present specification discloses sequence information for AIR. The disclosure additionally describes methods for determining the ability of polypeptide variants to inhibit induced cell death. The specification is very thorough in its description of methods for making analogues, mutants and variant polypeptide and DNA having homology to native AIR. Moreover, it cannot be disputed that such techniques are routine matters for persons having ordinary skill in the art and require no inventive thought or actions by the artisan. Furthermore, it should be mentioned that in this art the level of ordinary skill is very high. Therefore, knowledge of a variety of sophisticated techniques and methods is presumed. It requires only routine methodology to construct a DNA that encodes a polypeptide having similarity with a predetermined polypeptide; it also requires only routine methodology to test whether such polypeptide has the required activity. What is important is whether one of ordinary skill in this art will be required to use inventive thought in order to prepare and test the polypeptides. Mutagenesis procedures allowing thousands of DNA and polypeptide variants to be prepared and tested in an almost automated manner are known in the art. With such technology available there is little basis for arguing that preparing and testing vast numbers of variants involve undue experimentation. Thus, the present specification describes that which encompasses the claimed polypeptides and enables one of ordinary skill in the art to make polypeptides using routine procedures and determine which polypeptides would be operative, with no undue experimentation.

Further to the above remarks, the PTO has made it clear that the teaching required to support claims encompassing a number of molecules which are further limited by reciting an operable activity, is satisfied if the disclosure teaches how to make a candidate molecule and how to test the candidate molecule for the activity. *Ex parte Mark* 12 USPQ2d 1904 (Bd. Pat. App. & Int'f 1989). Applicants respectfully submit that the present specification describes that which encompasses AIR polypeptides and enables one of ordinary skill in the art to make polypeptides and DNA using routine procedures and determine which polypeptides would be operative, with no undue experimentation. Accordingly, the Examiner Section 112, first paragraph rejection is improper and should be withdrawn.

Further, with respect to new claims 22, 24 and 25 (relating to canceled claims 4, 5 and 18), the Examiner asserts that since the AIR polypeptide might comprise SEQ ID NO:2 plus extra amino terminus and/or an extra carboxy terminus, or might be any polypeptide having an amino terminus and a carboxy terminus selected from SEQ ID NO:2, one skilled in the art

would not know how to use a polypeptide having, for example SEQ ID NO:2 to which are fused an amino acid from position 1-29 and an amino acid from position 190-200. Applicants repeat the remarks presented above in connection with the standard of enablement under Section 112, first paragraph. With respect to claim 24, since any of amino acid residues 1-29 can be the N-terminus (the signal peptide) and any of amino acid residues 190-200 can form the carboxy terminus of the extracellular domain (as determined by computer modeling), there is no basis for the Examiner's assertion that one skilled in the art cannot make or use the claimed polypeptides. The ability of binding portions (extracellular domain) to inhibit signals mediated by a receptor binding to its ligand is a recognizable phenomenon. The Examiner assertion that one skilled in the art would not no how to use the claimed polypeptide has no bases. Similarly, claim 25 recites a DNA encoding a polypeptide that includes any of the amino acids of the termini of the cytoplasmic domain. For the same reasons stated above, this claim is enabled. Applicants submit that it requires only elementary and routine techniques to prepare fragments of the AIR extracellular or cytoplasmic domain. Additionally, it requires only routine testing to determine if the polypeptide fragment inhibits apoptotic cell death or mediates cell death. Applicants further repeat that the teaching required to support claims encompassing molecule fragments which are further limited by reciting an operable activity, is satisfied if the disclosure teaches how to make a candidate molecule and how to test the candidate molecule for the activity. *Ex parte Mark* 12 USPQ2d 1904 (Bd. Pat. App. & Int'f 1989). Since the present specification describes that which encompasses AIR polypeptides and enables one of ordinary skill in the art to make polypeptides and DNA using routine procedures and determine which polypeptides would be operative, with no undue experimentation, this Section 112, first paragraph rejection is improper and should be withdrawn.

Finally, the Examiner asserts that claim 2 recites nucleotides sequences that include those of SEQ ID NO:1 having modifications and one skilled in the art would not know how to make such molecules commensurate in scope with the claims, and how to use them. Applicants respectfully traverse this rejection and repeat the remarks presented above relating to the standard of enablement. Claim 2 recites fragments. As stated above, those skilled in the art are able to use only routine procedures well known in the art to prepare such oligonucleotides. What is more, as known in the art such oligonucleotides have far reaching usefulness as probes for probing DNA and primers for PCT reactions. These procedures are equally well known to one skilled in the art. In view of the above remarks, there is simply no basis for the Examiner's position that one skilled in the art would not know how to make or how to use the claimed fragments, and this rejection should be withdrawn.

Next the Examiner rejects claims 1-3, 6-7, 10-11, 13-14, and 16-17 under 35 U.S.C.§112, second paragraph, because the Examiner believes that these claims are indefinite. More particularly, the Examiner states that claims 1 and 3 are indefinite because

they recite the amino acid sequence of SEQ ID NO:5 and SEQ ID NO:5 is a nucleic acid. Applicants note that SEQ ID NO:5 also provides the deduced amino acid sequence. However, Applicants have amendment claims 1 and 3 to recite the amino acid sequence of SEQ ID NO:6.

Also, the Examiner states that claim 1 is indefinite, because it recites a DNA encoding a protein named AIR and that the name of a protein does not define it in terms of structure of function. Applicants have amended claim 1 to delete reference to and recite a specific function of the encoded polypeptide. Applicants submit that in view of this amendment, this rejection is overcome.

Further, the Examiner states that claim 1 is indefinite because it recites DNA capable of hybridizing under stringent conditions and the conditions are not stated in the claim. As amended, claim 1 incorporates the stringent conditions described on page 9 of the specification. The Examiner also asserts that the stringency conditions can allow for non-related molecules to hybridize, for example, because of wash conditions. Applicant disagrees with the Examiner position. The effect of the hybridization will be the result of the highest stringency used during hybridization and washing. The Examiner has provided no documentation or analysis to support the conclusion that "non-related molecules" will hybridize to the specifically recited sequences. Without such evidence, the Examiner's position is improper and without merit. Applicants request that the Examiner provide scientifically sound documentation. Additionally, Applicants submit that in the absence of such documentation, this rejection must be withdrawn.

Again, with respect to claim 1, the Examiner is of the opinion that it is indefinite because it recites biologically active AIR and that biologically active AIR is not so defined as to adequately describe a function peculiar to AIR. Applicants disagree with the Examiner and direct the Examiner's attention to the specification page 4, last paragraph. Nevertheless, in order to expedite prosecution of this claim, Applicants have amended claim 1 to recite a specific AIR function.

The Examiner further asserts that claim 2 is indefinite because it is not clear what is meant by "a nucleotide sequence derived from the DNA of SEQ ID NO:1". While Applicants believe that the specification is clear on the meaning of derived (referring to "derivatives" of the sequence which are described beginning on page 7, third full paragraph,), Applicants have amended claim 2 to recite oligonucleotides that are fragments of DNA of SEQ ID NO:1. As discussed above, such fragments are useful as probes and primers.

With respect to claim 3, 16, 17 and 18, these claims are rejected because of the use of the term "biologically active AIR", biologically active fragments" and stringent conditions" for the same reasons discussed above for claim 1. Claims 3, 16, and 17, are amended to specify hybridization conditions and recite specific biological activity. As for claim 18, this

claim is canceled and new claim 22 presented in its place. Applicants believe that in view of these amendments, this rejection is overcome.

In another Section 112, second paragraph rejection, the Examiner rejects claims 3 and 17 as being indefinite with respect to their recitation of a polypeptide that is at least about 70% identical to a specific amino acid sequence. Applicants have amended claims 3 and 17 to specify the algorithm for determining "percent identity". Support for this amendment is found on page 9, beginning at line 26. In view of this amendment, Applicants respectfully submit that one skilled in the art is able to determine what is meant by "70% identity" and this rejection should be withdrawn.

Applicants acknowledge the Examiner's comments relating to dependent claims 6, 7, 10, 11, 13, and 14 and submit that these claims are now allowable in view of the above discussion. Applicants further acknowledge the Examiner's comments relating to claim 18 and submit that in view of canceled claim 18, this rejection is moot.

As for the Examiner's comments relating to antecedent basis for the AIR in claims 13-15, Applicants have amended these claims to remove reference to AIR. In view of this amendment, this rejection is overcome.

Turning to the prior art rejection, the Examiner rejects claims 1-3, 6, 7, 10, 11, 13, 14, 15, 16 and 17 under 35 U.S.C. 103(a) as being unpatentable over Hillier et al., The WashU-Merck EST project, EST NCBI Accession H46211 or H46374, July 31, 1995. The Examiner asserts that the EST fragment H46211 has stretches of, for example, 116 nucleotides identical to SEQ ID NO:1 (position 90-205), and is overall 95.7% identical to SEQ ID NO: 1 from position 90-436. The Examiner states that such EST fragments encode a protein comprising biologically active fragments of AIR, for example, an epitope of AIR. Applicants traverse this rejection on the grounds that these ESTs neither teach nor suggest the presently claimed sequences or the claimed sequence fragments having the claimed activity. Moreover, these ESTs provide no motivation for one skilled in the art to make the present invention with any expectation of success.

The Examiner asserts that EST H46211 has nucleotides that are identical to 116 nucleotides SEQ ID NO:1 (nucleotides 663-778). The Examiner goes on to say that EST H46211 is overall 95.7% identical to nucleotides 440-778 of SEQ ID NO:1. These fragments of SEQ ID NO:1 are out of frame and taken by themselves are meaningless because they provide no information as to any polypeptide that the EST may encode. Thus, this EST provides nothing more than a short segment that has homology with a portion of the present invention. As for EST H46374, this nucleotide fragment also provides fragments having identity with portions of the presently disclosed nucleotide sequence, but these fragments are out of frame and are meaningless because the provide no information as to any polypeptide that the EST may encode. There is nothing in the cited ESTs that remotely suggests an open reading frame that encodes a polypeptide having the recited activity. There is nothing in the

cited references that remotely suggests an amino acid fragment that has the recited activity. Applicants submit that in view of the above remarks and the amended claims this rejection is overcome and should be withdrawn.

In view of the foregoing amendment and remarks, Applicants respectfully submit that the claims pending in this application are now in condition for allowance and a notice to that effect is respectfully requested.

Respectfully submitted,

Janis C. Henry

Janis C. Henry
Attorney for Applicant
Reg. No. 34,347

Immunex Corporation
Law Department
51 University Street
Seattle, WA 98101
Telephone: (206) 587-0430

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date indicated below.

Date: Dec. 21, 1998 Signed: Janice M. Kertson